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Nuts and Berries for Heart Health

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Abstract Nuts are nutrient-dense foods with complex matrices rich in unsaturated fatty acids and other bioactive compounds, such as L-arginine, fiber, minerals, tocopherols, phytosterols, and polyphenols. By virtue of their unique composition, nuts are likely to beneficially impact heart health. Epidemiologic studies have associated nut consumption with a reduced incidence of coronary heart disease in both genders and diabetes in women. Limited evidence also suggests beneficial effects on hypertension and inflammation. Interventional studies consistently show that nut intake has a cholesterol-lowering effect and there is emerging evidence of beneficial effects on oxidative stress, inflammation, and vascular reactivity. Blood pressure, visceral adiposity, and glycemic control also appear to be positively influenced by frequent nut consumption without evidence of undue weight gain. Berries are another plant food rich in bioactive phytochemicals, particularly flavonoids, for which there is increasing evidence of benefits on cardiometabolic risk that are linked to their potent antioxidant power.

Keywords Tree nuts · Peanuts · Berries · Fatty acids · Phytochemicals · Antioxidants · Flavonoids · Healthy diets · Epidemiologic studies · Clinical trials · Coronary heart disease · Stroke · Obesity · Metabolic syndrome · Visceral adiposity · Type 2 diabetes · Weight gain · Hypertension · Blood cholesterol · Triglycerides · Glycemic control · Insulin · Oxidation · Inflammation · Flow-mediated dilatation

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Introduction

Extensive research has been carried out on nuts and health outcomes since the 1992 publication of a landmark report from the prospective Adventist Health Study showing an association of nut consumption with a lower risk of coronary heart disease (CHD) [1]. This was soon followed by publication of a seminal clinical trial demonstrating that a diet enriched with walnuts reduced serum cholesterol levels compared with a standard healthy diet [2]. The interested reader will find updated information regarding nutrient contents, consumption patterns, and epidemiologic and clinical research on nuts and health outcomes in a 2006 monograph [3] and in a supplement collecting the proceedings of the 2007 Second International Nuts and Health Symposium [4].

The most popular edible tree nuts are almonds, hazelnuts, walnuts, pistachios, macadamias, and cashews. The consumer definition also includes peanuts, which botanically are legumes but have a nutrient profile similar to tree nuts. Nuts are energy-dense foods that are particularly rich in fat, mostly unsaturated fatty acids (Table 1); they also contain substantial amounts of fiber, folate, minerals, and antioxidants (both tocopherols and polyphenols) [3, 4]. These particular plant foods have been a marginal source of energy in Western diets, except for vegetarians and other health-conscious groups. However, nut consumption has increased in recent times following both the inclusion of this food group in guidelines for healthy eating and wide media coverage of recent evidence relating nut intake to a wide range of health benefits. Because of the link of nut consumption with a reduced risk of both CHD and intermediate biomarkers, such as blood cholesterol, the US Food and Drug Administration issued a health claim for nuts in the summer of 2003 [5]. Since then, nuts have become an indispensable component of heart-healthy diets, as reviewed in this journal as recently as 2007 [6].

Berries are a group of fruits that are not particularly consumed by most Western populations in spite of their health benefits, as documented in emerging research [7••]. In contrast to nuts, berries are low in calories, devoid of fat, and high in moisture. They also contain many bioactive substances, such as fiber, vitamin C, folate, and minerals, and are particularly rich in polyphenols, particularly flavonoids (anthocyanins and procyanidins) [8]. Anthocyanins comprise the largest group of natural, water-soluble plant pigments and impart the bright colors to berry fruits and to flowers. Besides specific associations between consumption of berries or berry flavonoids and cardiovascular outcomes in prospective studies, clinical trials have shown the potential of consuming berries to improve intermediate markers of heart disease in relation to their support for antioxidant mechanisms [7••, 8].

In this review, we summarize recent knowledge on the expanding area of nuts and berries and heart health. Effects of consumption of these special foods on related outcomes, such as obesity and diabetes, and other health aspects will also be addressed.

Nuts and Risk for Cardiovascular Disease

Prospective epidemiologic studies conducted over the past two decades in the United States (US) and across Europe have consistently shown an association between the increased frequency of nut intake and reduced risk of CHD [9]. Nut consumption continues to be the focus of intense research within prospective studies exploring specific clinical cardiovascular end points (i.e., fatal CHD, type 2 diabetes, stroke, heart failure, and hypertension) and in controlled feeding studies exploring intermediate biomarkers of cardiovascular disease risk.

Prospective Studies with Clinical Endpoints

A summary of the data from the Adventist Health Study, Iowa Women's Health Study, Nurses' Health Study (NHS), and Physician's Health Study (PHS) was conducted using the median of each nut consumption category associated with the relative risk of fatal CHD [10]. A distinct dose-response gradient existed in each study and an 8.3% reduction in risk of CHD death was estimated for each weekly serving of nuts. A recent pooled analysis of these 4 US cohort studies showed a relative risk (RR) of 0.65 (95% CI, 0.47–0.89) for CHD mortality between participants who ate nuts at least twice per week compared with those who never or rarely consumed nuts [11•].

Table 1 Energy and fat content and average fatty acid and sterol composition of nuts per 28-g serving

Nuts[a]	Energy, *kcal*	Fat, *g* (% En)	SFA, *g*	MUFA, *g*	PUFA, *g*	LA, *g*	ALA, *g*	PS, *mg*
Almonds	162	14.2 (78.9)	1.1	9.0	3.4	3.4	0.0	33.6
Brazil nuts (dried)	183	18.6 (91.5)	4.2	6.9	5.8	5.7	0.0	NR
Cashews	154	13.0 (76.0)	2.6	7.6	2.2	2.2	0.0	44.2
Hazelnuts	176	17.0 (86.9)	1.3	12.8	2.2	2.2	0.0	26.9
Macadamia nuts	201	21.2 (94.9)	3.4	16.5	0.4	0.4	0.1	32.5
Peanuts	149	13.8 (83.4)	1.9	6.8	4.4	4.4	0.0	61.6
Pecans	193	20.2 (94.2)	1.7	11.4	6.0	5.8	0.3	28.6
Pine nuts (dried)	188	19.2 (91.9)	1.4	5.3	9.5	9.3	0.0	39.5
Pistachios	156	12.4 (71.5)	1.5	6.5	3.8	3.7	0.1	59.9
Walnuts	183	18.3 (90.0)	1.7	2.5	13.2	10.7	2.5	20.2

[a] Data are for raw nuts, except when specified

ALA α-linolenic acid; *En* energy; *LA* linoleic acid; *MUFA* monounsaturated fatty acids; *PS* plant sterols; *PUFA* polyunsaturated fatty acids; *SFA* saturated fatty acids.

Data from US Department of Agriculture [60]

Although previous findings from the NHS suggested that nut and peanut butter consumption was associated with a reduced incidence of type 2 diabetes in women [12], no association between nut consumption and type 2 diabetes was found in male participants in the PHS cohort [13]. In light of the heightened risk of cardiovascular disease (CVD) among persons with diabetes, investigators further evaluated the relationship between nut consumption and CVD (including CHD and stroke) among women with type 2 diabetes enrolled in the NHS and found a lower risk of CVD (RR=0.56; 95% CI, 0.36–0.89) [14]. Alternatively, no association between the frequency of nut intake and ischemic stroke [15] and risk of heart failure [16] was found in the PHS cohort, yet a J-shaped relationship was found between nut consumption and hemorrhagic stroke [15]. However, there were a limited number of hemorrhagic strokes in the highest categories of nut consumption, thus further studies are clearly warranted to confirm or discard this improbable adverse effect of nuts.

Prospective Studies of Nut Consumption and Hypertension

Two prospective studies have assessed the frequency of nut consumption in relation to incident hypertension with discordant results [17, 18]. In a cohort of 15,966 participants in the PHS [17] who were free of hypertension at baseline and had 237,585 person-years of follow-up, adjusted hazard ratios for hypertension ranged from 0.97 (95% CI, 0.91–1.03) for nut consumption 1 to 2 times per month to 0.82 (95% CI, CI, 0.71–0.94) for nut consumption of 7 or more times per week. In a secondary analysis stratified by body mass index (BMI), there was an inverse relationship between nut intake and hypertension in lean participants but not in those who were overweight or obese at baseline. These results must be taken with caution, however, because salt intake and changes in weight, two major factors that influence the risk of hypertension, were not accounted for in this study. The second study, which involved 9919 Spanish university graduates followed-up for a median of 4.3 years in the Seguimiento Universidad de Navarra (SUN) cohort [18], found no association between nut consumption and incidence of hypertension after adjusting for several confounders, including exposure to salt and weight changes during follow-up. The hazard ratio for the highest versus lowest nut-consumption category was 0.77 (95% CI, 0.46–1.30) in this relatively young sample of well-educated adults at little baseline risk for hypertension, thus a larger sample and longer duration of follow-up might have provided a better level of evidence. In summary, limited epidemiologic data provide only circumstantial evidence for a protective effect of nut consumption on the development of hypertension.

Nut Consumption and Inflammatory Markers in Epidemiologic Studies

Because inflammation is a key process in atherogenesis, one mechanism by which nut consumption may decrease CHD risk is by improving inflammatory status, which can be estimated from levels of circulating biomarkers. Three cross-sectional studies have investigated nut consumption in relation to circulating inflammatory biomarkers [19–21]. In an analysis of data from nearly 6000 participants in the Multi-Ethnic Study of Atherosclerosis, consumption of nuts and seeds was inversely associated with levels of inflammatory markers, C-reactive protein (CRP), interleukin-6 (IL-6), and fibrinogen [19]. Another study of 987 diabetic women from the prospective NHS showed a direct association between nut consumption and increased plasma levels of adiponectin, an adipose tissue-secreted cytokine with anti-inflammatory and anti-atherosclerotic properties [20]. The third study was carried out in 772 older individuals at high risk for CHD living in Spain with the purpose of assessing adherence to the Mediterranean dietary pattern and its food components in relation to levels of soluble inflammatory markers. Adjusted mean serum levels of intercellular adhesion molecule-1 (ICAM-1), but not those of CRP or IL-6, decreased across increasing tertiles of nut consumption [21].

Nut Feeding Studies with Outcomes on Intermediate Markers

Lipids

The effects of nut consumption on blood lipids and lipoproteins have been investigated in over 40 nut intervention trials to date. A recent pooled analysis of 25 clinical studies conducted in seven countries examining nut-enriched diets versus control diets for outcomes on blood lipids found that nuts had a cholesterol-lowering effect that was dose-related, similar by gender, relevant across all age groups, and independent of the type of nut tested [22••]. Specifically, consumption of 67 g (2.4 oz) of nuts daily produced estimated mean reductions of 10.9 mg/dL (5.1%) in total cholesterol, 10.2 mg/dL (7.4%) in low-density lipoprotein (LDL) cholesterol, and 0.22 mg/dL (8.3%) in LDL to high-density lipoprotein (HDL) ratios ($P<0.001$ for all). Nuts had no significant effect on HDL cholesterol or triglycerides, except in participants with serum triglycerides higher than 150 mg/dL, in whom a significant 10.2-mg/dL reduction was observed. Importantly, participants with high baseline LDL cholesterol levels (>130 mg/dL) and lower BMI (<25 kg/m^2) (Fig. 1), as well as those consuming Western diets, experienced more pronounced lipid-lowering effects from nut consumption. Although the cholesterol-

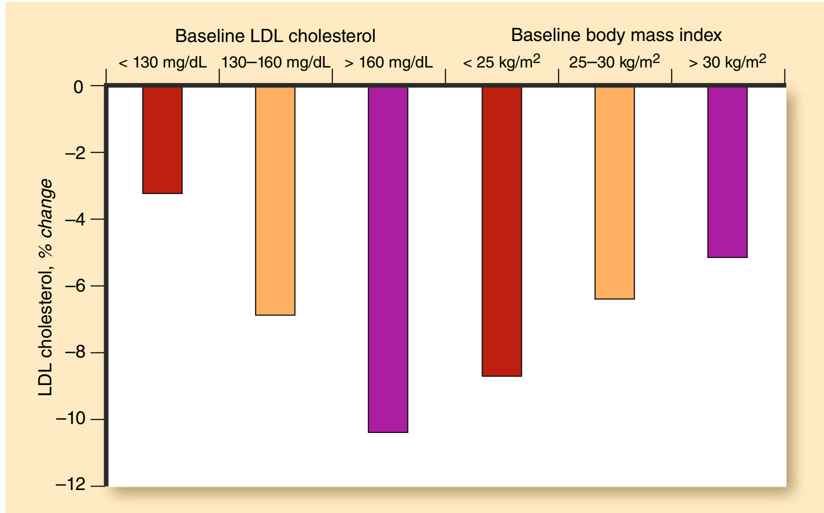

Fig. 1 Low-density lipoprotein (LDL) cholesterol response to nut feeding by baseline LDL cholesterol level and body mass index (BMI). Data from a pooled study of 25 nut-feeding trials in which the mean serving size was 67 g (2.4 oz) of nuts per day (*Adapted from* Sabaté et al. [22••])

lowering effect is consistent with results from prior individual clinical trials, the observed interaction between nut consumption and BMI was a novel finding.

There may be reasons for decreased lipid responsiveness to nut diets in overweight or obese persons and those with metabolic syndrome (MetS). Studies have shown that the LDL cholesterol response to diets low in saturated fatty acids [23] or to egg feeding as dietary cholesterol challenge [24] are blunted in obese, insulin-resistant individuals compared with lean, insulin-sensitive individuals. It has also been reported that higher BMI is associated with decreased LDL cholesterol responses to hypolipidemic diets [25]. High cholesterol synthesis and reduced intestinal cholesterol absorption in insulin-resistant states [26] might explain these findings, as an enhanced cholesterol flux through the liver will down-regulate LDL receptors and make them refractory to additional regulation by dietary fatty acid changes, whereas a decreased cholesterol flux though enterocytes would lessen both the cholesterol-raising response to dietary cholesterol and the cholesterol-lowering effect of plant sterols. Nuts are rich in plant sterols, which are likely to contribute to their cholesterol-lowering effect [27], but this would be less operative when cholesterol absorption is low. Recently, suggestive evidence has been provided that phytosterols in nuts relate to the LDL cholesterol response observed after their consumption [28]. Of note, two recent randomized trials that tested diets enriched in cashews or walnuts [29] and mixed nuts [30] compared with control diets in obese patients with metabolic syndrome failed to show the predictable cholesterol lowering effect, which supports the findings of the pooled analysis of and inverse association between the blood lipid response to nuts and BMI [22••].

In light of the unique composition of walnuts, the fatty fraction of which is particularly rich in polyunsaturated fatty acids (linoleic and α-linolenic acids) [3], a separate meta-analysis of 13 clinical studies was conducted by Banel and Hu [31••] to explore the effect of walnut-enriched diets on blood lipid levels. Compared with control diets, diets containing walnuts in amounts varying from 30 to 108 g/d (10–24% of energy) were associated with weighted mean reductions of total cholesterol and LDL cholesterol of 10.3 mg/dL and 9.2 mg/dL ($P<0.001$ for both), respectively, which concur with the results of the pooled analysis for different nut types [22••]. Recent well-controlled clinical trials using walnut diets against control diets confirm the cholesterol-lowering efficacy of walnuts [32–35]. Because the interventions ranged from 4 to 8 weeks in most studies, Torabian et al. [34] investigated if the short-term lipid effects of walnut consumption (12% of energy) could be maintained and extended to a 6-month period in 87 free-living individuals to whom no dietary advice was given. The inclusion of walnuts as part of the habitual diet reduced total cholesterol by 5 mg/dL ($P=0.02$) and triglycerides by 8 mg/dL ($P=0.03$), with a nearly significant decrease of 3.5 mg/dL in LDL cholesterol ($P=0.06$). Consistent with the results of the pooled analysis [22••], the lipid-lowering effects of walnuts were found to be more pronounced among participants with higher baseline LDL cholesterol. Furthermore, Tapsell et al. [35] tested a walnut diet against a control diet for up to 1 year in obese patients with diabetes and showed maintained, albeit small, LDL cholesterol reductions and HDL cholesterol increases with the walnut diet.

Blood Pressure

No discernible effect of nut feeding on blood pressure has been observed in the usually small-sized clinical studies performed to date with main outcomes on changes of the lipid profile, but the larger Prevencion con Dieta

Mediterranea (PREDIMED) trial did show significant reductions in both systolic and diastolic blood pressure in high-risk participants after 3 months of a Mediterranean diet supplemented with 30 g/d of mixed nuts compared with the control diet, but not with a Mediterranean diet supplemented with virgin olive oil [36]. A recent report from this study provides an insight into the possible mechanism of this antihypertensive effect by showing that both the nut-enriched and olive oil–enriched diets were associated with a reduced cholesterol to phospholipid ratio of erythrocyte membranes, which would translate into increasing membrane fluidity [37•]. Adequately powered future studies may uncover a true antihypertensive effect of nut intake.

Emerging Risk Factors for Cardiovascular Disease

By virtue of their unique fat and nonfat composition, nuts are likely to affect markers of atherogenesis other than the lipid profile or carbohydrate metabolism. More recently, the effects of nuts on novel CHD risk factors have been evaluated, including oxidative stress, inflammation, and vascular reactivity [6, 38••, 39•]. The emerging picture is that frequent nut consumption has beneficial effects on cardiovascular risk factors beyond well-established cholesterol lowering.

Regarding oxidation, nuts are important sources of tocopherols and phenolic compounds with potent antioxidant effects, as shown by reduction of lipid peroxidation or oxidative DNA damage with nut extracts in studies in vitro and the beneficial effects of nut intake on lipid oxidation, antioxidant enzyme activity, and formation of cholesterol oxidation products in both acute and chronic experimental animal studies [38••, 40]. Oxidative markers after feeding of monounsaturated fatty acid (MUFA)-rich nuts, predominantly almonds, have been examined in several randomized feeding studies, usually of small size and lasting from 3 to 8 weeks [39•]. Biomarkers of oxidation were secondary outcomes in most of these studies, which showed inconsistent results, with either reduced or unchanged oxidation, but in no case was there worse oxidative status compared with various control diets. Several feeding studies of similar characteristics have assessed oxidative biomarkers after consumption of diets supplemented with polyunsaturated fatty acid (PUFA)-rich walnuts versus other healthy diets [38••]. In general, there were no between-diet differences in oxidative status. In the higher statistically powered PREDIMED trial, a Mediterranean diet enriched with 30 g of mixed nuts given daily for 3 months to older individuals at high cardiovascular risk resulted in a lower oxidized LDL level compared with a control diet, but not with a virgin olive oil–enriched diet [41•]. Available evidence suggests that MUFA-rich nuts may moderately improve oxidative status, whereas PUFA-rich nuts (walnuts) have a neutral or slightly beneficial effect, but no studies have shown that frequent nut consumption reduces antioxidant defenses.

With respect to inflammation, the high content of phenolic compounds in nuts, particularly in the pellicle (outer skin), might anticipate an anti-inflammatory effect of frequent nut consumption, as suggested in cross-sectional studies [19–21]. Nevertheless, plasma levels of CRP, a standard measure of systemic low-grade inflammation, were usually unaffected in controlled feeding trials (as reviewed up to 2008) with almonds, walnuts, or mixed nuts [38••]. It must be noted that inflammatory biomarkers were always secondary outcomes of nut feeding trials; thus, statistical power to detect significant changes is a problem. A further substudy of the PREDIMED trial analyzed both 3-month changes in circulating inflammatory biomarkers and in the expression of ligands for inflammatory molecules in circulating monocytes after the study diets, one of which was supplemented with 30 g/d of mixed nuts [42•]. The findings indicate reductions in both circulating inflammatory mediators and, importantly, reduced monocyte expression of pro-inflammatory ligands after both olive oil–enriched and nut-enriched Mediterranean diets compared with the control diet, thus beginning to unravel the molecular bases for the anti-inflammatory effects of nut consumption.

Concerning vascular reactivity, both walnut diets and walnut meals had shown improved flow-mediated dilatation (FMD) in the brachial artery in two earlier studies conducted in healthy and hypercholesterolemic patients [38••]. A recent cross-sectional study in diabetic patients compared a walnut diet with an isoenergetic ad libitum diet with similar saturated fatty acid (SFA) content without walnuts, each lasting 8 weeks, and confirmed that walnuts improve FMD [33]. This beneficial effect of walnuts may be ascribed, in part, to their high content of PUFA, antioxidants, and L-arginine, the precursor of nitric oxide, which is an endogenous vasodilator. Although there is a paucity of vascular reactivity studies after consumption of diets enriched with nuts other than walnuts, they might be expected to show similar beneficial effects because all nuts contain substantial quantities of bioactive compounds that can favorably influence vascular reactivity. This is a key area for future research.

Does Nut Consumption Promote Obesity?

Nuts are high-fat, energy-dense foods, which are attributes usually linked to weight gain. However, past epidemiologic studies do not support the concern that nut consumption might promote weight gain [3, 4, 6]. Consistent with prior epidemiologic findings in the United States, the SUN study (8800 adult men and women) found that participants who consumed nuts frequently (≥2 times per wk) had a 40% reduced risk of weight gain (odds ratio of 0.61; 95% CI, 0.47–0.79) during a 28-month follow-up [43•]. Notably, SUN was the first epidemiologic study that evaluated the direct effect of nut consumption on body weight in a prospective manner, and has provided evidence that frequent nut consumption is not associated with an increase in body weight, change in body weight, or incidence of overweight or obesity over time. Bes-Rastrollo et al. [44•] recently investigated the relationship between nut consumption and long-term weight change after an 8-year follow-up in 51,188 women from the NHS cohort. Using multivariate analysis controlling for lifestyle and other dietary factors, frequent nut consumption (≥ 2 times per week) was associated with a lower risk of obesity (hazard ratio of 0.77; 95% CI, 0.57–1.02; *P* for trend= 0.003). Furthermore, in a cross-sectional study of a sample of 847 individuals recruited into the PREDIMED study, nut consumption was inversely associated with adiposity measures (BMI and waist circumference) independently of other lifestyle variables. From regression coefficients of nut intake versus adiposity variables, it was predicted that BMI and waist circumference decreased by 0.78 kg/m^2 and 2.1 cm, respectively, for each daily serving of 30 g of nuts [45].

Several small clinical studies in free-living individuals explored the association between moderate nut consumption and body weight as a main outcome and showed no overall increase in body weight, as reviewed [3, 4, 6]. Recent evidence from the PREDIMED study shows a decreased prevalence of the MetS, mainly due to reduced visceral adiposity, after intervention for 12 months in participants following a Mediterranean diet supplemented with 30 g of nuts per day [46•]. Other clinical trials have suggested that almonds and other nuts may favor weight loss within energy-restricted diets, possibly by increasing compliance, but enhanced satiety, increased thermogenesis, and fat malabsorption, documented as increased fecal fat excretion in several nut studies, could also be contributing factors [47].

Effects of Nuts on Glycemic Control

Type 2 diabetes is a condition of metabolic decline with an increased risk of cardiovascular disease. Consuming nuts in an otherwise healthy diet may help to alleviate this condition by providing key nutrients that have an impact on disease processes, such as unsaturated fatty acids and compounds with antioxidant activity. Dietary fat, for example, has been shown to influence insulin action through mechanisms associated with cell membrane structure and possibly signaling [48].

As discussed, the epidemiologic evidence on nut consumption and diabetes risk is contradictory, with benefits suggested for women [12] but not men [13]. Some interventional studies have examined the effects of nut-enriched diets on glycemic control in diabetic patients and insulin sensitivity in insulin-resistant states. Earlier studies had shown inconsistent effects of nut-enriched diets on fasting or postprandial glucose and hemoglobin A1C in patients with diabetes or in insulin sensitivity in patients with obesity or MetS, as reviewed [3, 4, 6]. Two recent, small 3-month studies, however, found reduced insulin levels in obese Spanish patients with metabolic syndrome given 30 g/d of mixed nuts [30] and in obese Australian patients with diabetes consuming 30 g/d of walnuts [35]. The 3-month report of the larger PREDIMED study [36] also showed that the Mediterranean diet enriched with nuts was associated with improved insulin sensitivity and fasting glucose levels in non-diabetic and diabetic participants, respectively. In a shorter crossover study of 1-month in duration in 27 hyperlipidemic Canadians, an effect was seen with 36 g/d and 73 g/d of almonds in a low-fat background diet and a diet using muffins as control foods [49]. Both almond diets were associated with decreased 24-h urinary C-peptide, an indirect measure of insulin secretion. The consistency of the results in different populations adds strength to the evidence of a beneficial effect of nuts on pathways related to the development of diabetes.

Given a possible contributory effect of unsaturated fats in nuts, these results are consistent with associations described between dietary fats and diabetes risk [50••]. Other components in nuts, such as phenolic compounds, may also provide protection by effecting intermediate markers of the disease, such as improved FMD after a walnut diet in obese patients with type 2 diabetes [33]. Indeed, nuts deliver multiple bioactive constituents besides unsaturated fatty acids [27], which may well address a number of processes in the causal pathway to degenerative diseases such as diabetes. Shorter-term studies have shown acute beneficial effects of nut meals. For example, adding almonds to a meal of white bread was found to reduce the meal glycemic index in a dose-dependent manner [51]. Reduced glycemic excursions mean lesser demands on insulin secretion, which is a key factor in the development of diabetes. Another acute study from the same group found less oxidative protein damage when postprandial glucose excursions were ameliorated by almond consumption [52]. Taken together, these studies help form a better understanding of how nut consumption may be beneficial in creating conditions to combat diabetes.

Berries and Heart Health

There is an emerging body of science demonstrating the impact of berry consumption on cardiovascular health. A recent review of clinical studies published in the period 1998 from 2009 found that the constituents of berries, namely polyphenols, vitamins, minerals, and fiber, are linked to improved cardiovascular risk profiles [7••]. This article examined 20 dietary studies using different berries and in different forms, with main effects relating to improvements in serum antioxidant status and reduced oxidized lipid fractions. These effects could be attributed to compounds with antioxidant capacity, in particular vitamin C and anthocyanin flavonoids, which are variably enriched in different berries [8], a reason why different effects could be observed depending on the type of berry consumed [7••]. Beneficial effects on glucose homeostasis, lipid metabolism, and blood pressure were also noted to varying degrees, as would also be expected.

From the studies reviewed, and notwithstanding differences in study design, the relatively consistent findings on oxidative status likely reflect the main protective element deliverable in berries [7••]. For example, in one study of 30 healthy men, increasing daily doses of cranberry juice over three 4-week periods were associated with significant reductions in oxidized LDL concentrations, which were accompanied by decreased levels of circulating cell adhesion molecules [53]. These results contrasted with those of an earlier study involving healthy young women consuming 750 mL/d of cranberry juice that showed no effects on blood antioxidant status or oxidative DNA damage [54], but the differences may have related to the study population, conditions of the test beverage, and outcome measures. Recent randomized clinical studies have related consumption of mixed berries (bilberries, lingonberries, strawberries, and black currants) to increased plasma concentrations of polyphenols and vitamin C, reduced blood pressure, increased HDL cholesterol, and inhibition of platelet function [55] and to reduced alanine aminotransferase levels as a marker of fatty liver-related inflammation in MetS [56]. Acute effects from berry meals are also detectable, as shown by a recent meal test study showing delayed and attenuated glycemic responses resulting from adding berries (black currants, bilberries, cranberries and strawberries) to a sugar load [57].

The value of berry consumption in influencing oxidative status is becoming clearer with a greater understanding of the pathways involved in cardiovascular disease and the role of dietary chemical constituents in modulating related processes [7••, 58]. For example, in vitro and cell culture analyses of the bioactivity of berries traditionally consumed by native North Americans (highbush cranberry, chokecherry, silver buffaloberry, and serviceberry) found an array of beneficial effects, including improved glucose utilization, modulation of lipid metabolism and energy expenditure, and inhibition of pro-inflammatory gene expression associated with the inflammation seen in type 2 diabetes [59•].

In summary, berries deliver substantial amounts of vitamin C, flavonoids, and other potent chemicals with antioxidant effects and there is an increasing body of evidence that they are beneficial to health. In particular, berries have a positive influence on oxidative status and mechanisms associated with the low-grade systemic inflammation that underpins the progress of diabetes and cardiovascular disease. Long-term studies of dietary patterns that include substantial amounts of berries in an otherwise healthy diet may be required to confirm the contribution of berry consumption to the prevention of diabetes and cardiovascular diseases.

Conclusions

Nuts are energy-dense foods rich in bioactive macronutrients, micronutrients, and phytochemicals. The unique composition of nuts is critical for their effects on heart

Table 2 Effects of nut consumption on cardiovascular diseases and risk factors: summary of scientific evidence

Disease/factor	Effect	Level of evidence
Epidemiologic studies		
Coronary heart disease	Decrease	++
Ischemic stroke	No change	+
Heart failure	No change	+
Hypertension	Decrease	+/−
Diabetes	No change/decrease	+/−
Inflammatory markers	Decrease	+
Body weight	No change/decrease	++
Clinical studies		
Blood lipid profile		
Total cholesterol	Decrease	++
LDL cholesterol	Decrease	++
HDL cholesterol	No change/increase	+
Triglycerides	No change/decrease	+
Insulin sensitivity	No change/increase	+/−
Blood pressure	No change/decrease	+/−
Oxidation	No change/decrease	+/−
Inflammation	No change/decrease	+/−
Vascular reactivity	Increase	+
Body weight	No change	++
Visceral adiposity	Decrease	+

+/−, equivocal evidence; +, limited evidence from a few studies; ++, evidence from several studies; *HDL* high-density lipoprotein; *LDL* low-density lipoprotein health. Indeed, there is consistent evidence from epidemiologic and clinical studies of the beneficial effects of nut consumption on risk of CHD as well as on diabetes in women, and on major and emerging cardiovascular risk factors, as summarized in Table 2. The evidence to date is convincing that including nuts in a healthy dietary pattern will extend its cardioprotective effects. Importantly, beneficial effects take place without undue weight gain, or even with reduced adiposity, and target multiple cardiovascular risk factors and mechanisms, which help explain why nuts reduce the risk for CHD. Understanding the underlying biological mechanisms of the effects of nuts on mediators of CHD, obesity, MetS, and diabetes should help in the design of diets that include nuts to maximally reduce chronic disease risk. Ongoing research such as the large, randomized PREDIMED trial (final results expected in 2012), where one daily serving of mixed nuts within the context of the Mediterranean diet is provided to participants at high cardiovascular risk in one arm of this long-term study [36, 41•, 46•], might eventually settle the critical issues of whether, in comparison with a healthy control diet without nuts, a healthy diet supplemented with one daily serving of nuts prevents cardiovascular events and development of other prevalent chronic diseases, including diabetes, cancer, and neurodegenerative disorders.

Berries are another example of a whole plant food rich in bioactive phytochemicals, although, contrary to nuts, they are a low-energy food. Research on berries is more recent and less abundant than in the case of nuts, but there is a growing body of evidence demonstrating their potent antioxidant power and ability to beneficially impact on various intermediate pathways of cardiometabolic risk.

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- • Of importance
- •• Of major importance

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